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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/125,814 | 08/26/1998 | MASAHIKO DOHI | Q51505 | 8214 |

7590 05/07/2003

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| EXAMINER | |
|---|---|
| WELLS, LAUREN Q | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1617 | 39 |

DATE MAILED: 05/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Applicati n No. 09/125,814 | Applicant(s) DOHI ET AL. | |
|---|---|---|---|
| | Examin r Lauren Q Wells | Art Unit 1617 | |

*-- The MAILING DATE of this communication appears on the c ver sheet with the corresp ndence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *19 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *51-67* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *51-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

Claims 51-67 are pending. The Amendment filed 2/19/03, Paper No. 38, cancelled claims 46-50 and 68-98 and amended claims 51-66.

### *Continued Examination Under 37 CFR 1.114*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/19/03 has been entered.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 51-67 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(i) Claim 67 recites the limitation "described in claim 46". There is insufficient antecedent basis for this limitation in the claim.

(ii) The term "strongly" in claim 51 (1st line of second to last paragraph) is a relative term which renders the claim indefinite. The term "strongly" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

(iii) The term "analogs" in claims 59, 61, 63 is vague and indefinite, as the metes and bounds of this claim are unascertainable. What are analogs of these compounds? The specification does not define this phrase and one of ordinary skill in the art would not be apprised of its meaning.

(iv) The phrase "insulin-like growth factors" in claims 59, 63 is vague and indefinite because the claim includes elements not actually disclosed (those encompassed by "like"), thereby rendering the scope of the claim unascertainable. See MPEP 2173.05(d).

Regarding this phrase, Applicant argues, "Applicant's re-submit herewith pages from Products for Life Science Research to support Applicants' position that the phrase. . .is a term of art". This argument is not persuasive, as Applicant has not provided such a submission.

(v) The phrase "calcitonin gene-related peptides" in claims 59, 63 is vague and indefinite. What compounds are encompassed by these claims? Chemically, what does the term "related" refer to? The specification does not define this phrase and one of ordinary skill in the art would not be apprised of its meaning.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 51-57, 59-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Suzuki (4,613,500).

The instant invention is directed toward a powdery composition comprising a drug, one or more water absorbing and gel forming base materials, and one or more water absorbing and water insoluble base material.

Suzuki is directed to a powdery composition for nasal administration that contains a polypeptide, a water-absorbing and water-insoluble base material and, optionally, a water-absorbing and water-soluble (gel-forming) base material (title, abstract and col. 4, lines 50-66). For crystalline cellulose, inter alia, as the water-insoluble base, see col. 4, lines 21-41. For hydropropylcellulose, inter alia, as the water-soluble (gel-forming)base, see column 5, lines 10-22. The amount of gel-forming base is from 0.1-60 wt.% based on the amount of water-insoluble base (col. 5, lines 22-25).

Suzuki discloses at column 5, lines 53-65 that the drug may be adhered to or dispersed in the water-insoluble base. Suzuki does not teach that the drug is adhered to or dispersed in the gel-forming base. Therefore, even with the addition of a gel-forming base, it is reasonable to expect that the drug would be more adhered to or dispersed in the water-insoluble base. The particle size of more than 90 wt.% of the resultant particles is 10-250 microns (col. 5, lines 26-28). This suggests that the average particle size of each component, water-insoluble base, gel-forming base and drug, is 10-250 microns, which is encompassed by and overlaps the instantly claimed particle size ranges. The molecular weight of the polypeptide used is from 1,000 to 300,000, preferably 1,000 to 150,000 (col. 2, lines 56-63).

Suzuki does not teach the amount of drug dispersed on or in the base materials or the viscosity of the hydroxypropyl cellulose. It is within the skill in the art to select optimal parameters in a composition in order to achieve a beneficial effect. In re Boesch, 205 USPQ 215

(CCPA 198). Therefore, absent evidence of unexpected results, the amount of drug dispersed on or in the base materials is not given patentable weight. Suzuki does not limit the viscosity of the hydroxypropyl cellulose used. Therefore, the disclosure of Suzuki encompasses hydroxypropyl cellulose with a viscosity as instantly claimed. Absent evidence of unexpected results obtain by using hydroxypropyl cellulose with the instantly claimed viscosity, this limitation is not considered critical to the invention.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to select an optimal amount of drug dispersed on or in the base materials, an optimal viscosity of hydroxypropyl cellulose and disperse or adhere the drug more one or in the water-insoluble base material in the compositions of Suzuki in order to obtain a sufficient dose of drug with increased absorption efficiency and because it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. In re Aller, 105 USPQ 233.

The Examiner respectfully points out that the instant claims are product-by-process claims. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). See MPEP 2113.

Claim 58 is rejected under 35 U.S.C. 103(a) as being unpatentable over Suzuki as applied to claims 51-57, 59-67 above, and further in view of Makino (5,262,871).

Suzuki is applied as discussed above. The reference does not teach non-peptide/non-proteinaceous drugs.

Makino teaches non peptide/non-proteinaceous drugs (col. 7, line 60 to col. 8, line 26) for use in powdery nasal compositions (col. 4, lines 11-13).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute a non-peptide/non-proteinaceous drug as taught by Makino in the composition of Suzuki because Makino teach peptide/proteinaceous drugs and non-peptide/non-proteinaceous drugs as interchangeable for use in powdery nasal compositions.

***Response to Arguments***

Applicant argues, "the Declaration was submitted to show that the compositions of Suzuki and the present invention are different and that because the compositions of Suzuki and the present invention are different, unexpected results are obtained by the present invention". This argument is not persuasive, as the Declaration provides no comparative data between the instant invention and that of Suzuki.

Applicant argues, "the passage pointed out by the Examiner appears to be directed to a composition where only a water-absorbing and water-insoluble base material is used. Therefore, Applicants submit that the disclosure is not directed to a composition that contains a water-absorbing and water-soluble base material, and that when a water-absorbing and water-soluble base material is added, the drug adheres more to the water-absorbing and water-soluble base material". This argument is not persuasive. The Examiner respectfully points out Suzuki et al. teach the benefits of combining the water-soluble base material and the water-insoluble base material and further teaches the benefits when the pharmaceutical composition is absorbed on the

water-insoluble base. Thus, one of skill in the art would have been motivated to combine the teachings of this reference to obtain a composition comprising a drug, a water-insoluble base, a water-soluble base, wherein the drug is dispersed more on the water-insoluble base material because of the expectation of achieving a product wherein the water-insoluble base is more soluble and the drug adheres to the nasal mucosa, allowing the drug to have high efficiency, see Col. 3, lines 63-Col. 4, line 12 and lines 51-66. Furthermore, it is respectfully pointed out that it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. In re Aller, 105 USPQ 233.

Applicant argues that the compositions of Suzuki are made differently and that "In order for more of the drug to adhere to the water-absorbing and water-insoluble base, strong mixing is required. However, Suzuki does not teach or suggest the strength of mixing". This argument is not persuasive. First, the Examiner respectfully points out that the instant claims are directed to a product and that arguing the method of making the product is not commensurate in scope with the instant claims. Second, the Examiner respectfully points out Applicant has not provided any data comparing the two products. Thus, while Applicant argues that she has unexpected results of the products, there is no data showing such unexpected results. Furthermore, the Examiner respectfully points out that there is motivation in Suzuki et al. to make such a composition, especially since Suzuki et al. teach high efficiency of drug release when the drug is administered via the water-insoluble base.

Applicant argues, "In this case, since the drug is freeze-dried with the water-absorbing and water-soluble base material, the drug adheres more to the water-absorbing and water-soluble

base than on ore in the water-absorbing and water-insoluble base material". This argument is not persuasive. The Examiner respectfully points out showings of fact are much preferred to statements of opinion. In re Oelrich, 198 USPQ 210, 215 (CCPA 1978).

Applicant argues, "Makino does not teach or suggest a powdery composition where a drug is unevenly dispersed on or in a water-absorbing and water-insoluble base material, and therefore". This argument is not persuasive, as Makino was merely relied upon to teach non-peptide/non-proteinaceous drugs.

The Examiner respectfully points out that it is applicant's burden to demonstrate unexpected results over the closest prior art. See MPEP 716.02, also 716.02 (a) - (g). Furthermore, the unexpected results should be demonstrated with evidence that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance. *Ex parte Gelles*, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992). Moreover, evidence as to any unexpected benefits must be "clear and convincing" *In re Lohr*, 137 USPQ 548 (CCPA 1963), and be of a scope reasonably commensurate with the scope of the subject matter claimed, *In re Linder*, 173 USPQ 356 (CCPA 1972).

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lauren Q Wells whose telephone number is (703) 305-1878. The examiner can normally be reached on M-F (7-5:30), with alternate Mondays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (703)305-1877. The fax phone numbers for

the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

lqw
March 24, 2003

SREENI PADMANABHAN
PRIMARY EXAMINER

4/4/03